

D⁵ The grafting of such macromonomers to the bulk substrate material surface through attachment at the reactive sites of a polymeric tie layer yields a hydrophilic layer having for example a so-called bottle brush-type structure (BBT) composed of tethered "hairy" chains. Such BBT structures in one embodiment comprise a long hydrophilic or hydrophobic backbone which carries relatively densely packed comparatively short hydrophilic side chains (called primary bottle brushes). Another embodiment relates to secondary bottle brushes which are characterized in that the hydrophilic side chains themselves carry densely packed hydrophilic "secondary" side chains. Polymer coatings of said primary and secondary BBT structures to a certain extent mimic highly water-retaining structures occurring in the human body, for example in cartilage or mucosal tissue. sk

F). Please amend the first paragraph on page 72, lines 1-11 as follows:

D⁶ The complete coating of the bulk material according to the invention consists (a) of at least a partial tie layer, one or more tie layers comprising polyelectrolytes and (b) of an outer coating which may be hydrophilic or which may comprise various other active agents such as anti-microbial agents, organoselenium or block-type copolymers wherein one block is LbL active and the other is not. When the outer coating is hydrophilic, it is obtained by grafting one or more hydrophilic monomers or macromonomers onto the surface, wherein the latter makes up at least 50 %, from about 75 to about 98 % and from about 80 to about 95 % of the total thickness of the fully hydrated coating. sk

REMARKS

In response to the **Notice of Non-Compliant Amendment** dated April 22, 2003, Applicant amended four paragraphs by canceling structural formula introduced in the Amendment A filed August 2, 2002 (i.e., A)-D) through this Amendment B).

The second paragraph on page 71, lines 11-22, has been amended to correct typos and more clearly describe the invention. The phrase "a tie layer" should be "a hydrophilic layer" as clearly shown by the teachings from the third paragraph on page 45 to the second paragraph on page 71, lines 11-22, namely how to graft a coating having a so-called bottle brush-type structure (BBT) composed of tethered "hairy" chains, on top of a polymeric tie layer on the surface of a bulk material. Such grafting techniques is disclosed in detailed in WO 99/57581, which has been incorporated by reference in its entirety (the third paragraph on page 45). The second paragraph on page 71, lines 11-22, summarizes these teachings.

The first paragraph on page 72, lines 1-11 has been amended to correct typos and more clearly describe the invention. In the sentence "When the outer coating is hydrophilic, such a tie layer is obtainable by grafting one or more hydrophilic monomers or macromonomers onto the surface, wherein the latter makes up at least 50 %, from about 75 to about 98 % and from about 80 to about 95 % of the total thickness of the fully hydrated coating", "a tie layer" should mean an outer coating which may be hydrophilic, preferably having a so-called bottle brush-type structure (BBT) composed of tethered "hairy" chains; and should be "it" or "the outer coating", as clearly shown by the teachings in the paragraphs immediately preceding this paragraph (from the third paragraph on page 45 to the second paragraph on page 71, lines 11-22, namely).

Attached hereto is a marked-up version of the changes made to the **specification** by the present amendment. The attached page is captioned "Version With Marking To Show Changes Made."

Should the Examiner believe that a discussion with Applicants' representative would further the prosecution of this application, the Examiner is respectfully invited to contact the undersigned. Please address all correspondence to Thomas Hoxie, Novartis Corporation, Corporate Intellectual Property, One Health Plaza, Bldg. 430, East Hanover, NJ 07936-1080. The Commissioner is hereby authorized to charge any other fees which may be required under 37 C.F.R. §§1.16 and 1.17, or credit any overpayment, to Deposit Account No. 19-0134.

Respectfully submitted,



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Date: May 6, 2003

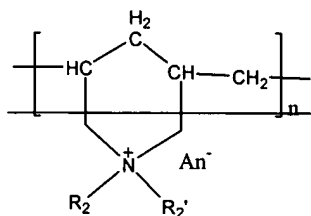
Novartis Corporation
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**Version with Markings to Show Changes Made****In the Specification:**

A). Please twice amend the paragraph beginning at page 30, line 4 and ending at page 31, line 13 as follows:

Further examples of synthetic cationic polymers useful in forming the tie layers of the present invention include:

- (i) a polyallylamine (PAH) homo- or copolymer, optionally comprising modifier units as described herein;
- (ii) a polyethyleneimine (PEI) as discussed above;
- (iii) a polyvinylamine homo- or copolymer, optionally comprising modifier units;
- (iv) a poly(vinylbenzyl-tri-C₁-C₄-alkylammonium salt), for example a poly(vinylbenzyl-tri-methyl ammonium chloride);
- (v) a polymer of an aliphatic or araliphatic dihalide and an aliphatic N,N,N',N'-tetra-C₁-C₄-alkyl-alkylenediamine, for example a polymer of (a) propylene-1,3-dichloride or -dibromide or p-xylylene dichloride or dibromide and (b) N,N,N',N'-tetramethyl-1,4-tetramethylene diamine;
- (vi) a poly(vinylpyridin) or poly(vinylpyridinium salt) homo- or copolymer;
- (vii) a poly (N,N-diallyl-N,N-di-C₁-C₄-alkyl-ammoniumhalide) comprising units of formula



wherein R₂ and R₂' are each independently C₁-C₄-alkyl, in particular methyl, and An⁻ is a, for example, a halide anion such as the chloride anion;

- (viii) a homo- or copolymer of a quaternized di-C₁-C₄-alkyl-aminoethyl acrylate or methacrylate, for example a poly(2-hydroxy-3-methacryloylpropyltri-C₁-C₂-alkylammonium salt) homopolymer such as a poly(2-hydroxy-3-methacryloylpropyltri-methylammonium chloride), or a quaternized poly(2-dimethylaminoethyl methacrylate or a quaternized poly(vinylpyrrolidone-co-2-dimethylaminoethyl methacrylate);

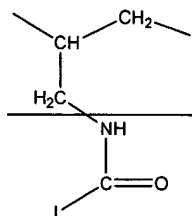
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(ix) POLYQUAD[®] as disclosed in EP-A-456,467; or

(x) a polyaminoamide (PAMAM), for example a linear PAMAM or a PAMAM dendrimer such as a amino-terminated Starbust[™] PAMAM dendrimer (Aldrich).

B) Please twice amend the paragraph beginning at page 31, line 22 and ending at page 32, line 7 as follows:

Suitable modifier units of the polyallylamine (i) are, for example, of formula



(5),

wherein L is C₂-C₆-alkyl which is substituted by two or more same or different substituents selected from the group consisting of hydroxy, C₂-C₅-alkanoyloxy and C₂-C₅-alkylamino-carbonyloxy.

L may be linear C₃-C₆-alkyl, such as linear C₄-C₅-alkyl, or, more particularly, n-pentyl which is in each case substituted as defined above.

C) Please twice amend the paragraph beginning at page 32, line 16 and ending at page 33, line 7 as follows:

A particular embodiment relates to polyallyl amines comprising units of the above formula (5), wherein L is a radical of formula

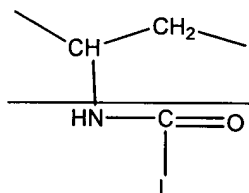


wherein g is 1, 2, 3, 4 or 5, preferably 3 or 4 and in particular 4, each R* is independently hydrogen or a radical -C(O)-R₂₉ or -C(O)-NH-R₂₉', and for R₂₉ and R₂₉' the above meanings and preferences apply. L is even more preferred a radical of the above formula (6) wherein g is 3 or 4, in particular 4,

and each group -OR* independently is hydroxy or hydroxy which is partly or completely acetylated, in particular hydroxy. Particular preferred radicals L are 1,2,3,4,5-pentahydroxy-n-pentyl or 1,2,3,4,5-pentahydroxy-n-pentyl wherein the hydroxy groups are partly or completely acetylated.

D) Please twice amend the paragraph bridging page 33 and page 34 as follows:

Suitable modifier units of the polyvinylamine (iii) are, for example, of formula



(5a),

wherein for L the above-given meanings and preferences apply.

A suitable polyvinylamine copolymer is, for example, a copolymer comprising vinylamine units and units derived from another hydrophilic comonomer, for example from acrylamide, N,N-dimethyl acrylamide, N-vinylpyrrolidone or the like.

E). Please amend the second paragraph on page 71, lines 11-22 as follows:

The grafting of such macromonomers to the bulk substrate material surface through attachment at the reactive sites of a polymeric tie layer ~~sites~~ yields a hydrophilic tie layer having for example a so-called bottle brush-type structure (BBT) composed of tethered "hairy" chains. Such BBT structures in one embodiment comprise a long hydrophilic or hydrophobic backbone which carries relatively densely packed comparatively short hydrophilic side chains (called primary bottle brushes). Another embodiment relates to secondary bottle brushes which are characterized in that the hydrophilic side chains themselves carry densely packed hydrophilic "secondary" side chains. Polymeric coatings of said primary and secondary BBT structures to a certain extent mimic highly water-retaining structures occurring in the human body, for example in cartilage or mucosal tissue.

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which may be hydrophilic or which may comprise various other active agents such as anti-microbial agents, organoselenium or block-type copolymers wherein one block is LbL active and the other is not. When the outer coating is hydrophilic, ~~it such a tie layer~~ is obtainable by grafting one or more hydrophilic monomers or macromonomers onto the surface, wherein the latter makes up at least 50 %, from about 75 to about 98 % and from about 80 to about 95 % of the total thickness of the fully hydrated coating.